2021 STI Treatment Guidelines

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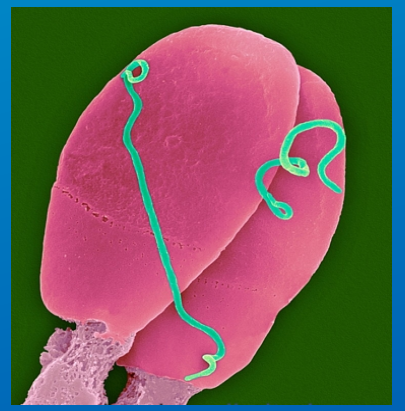
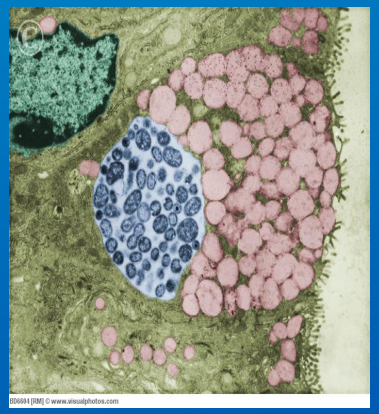
Clinical Associate Professor, University of WA
August 25, 2021

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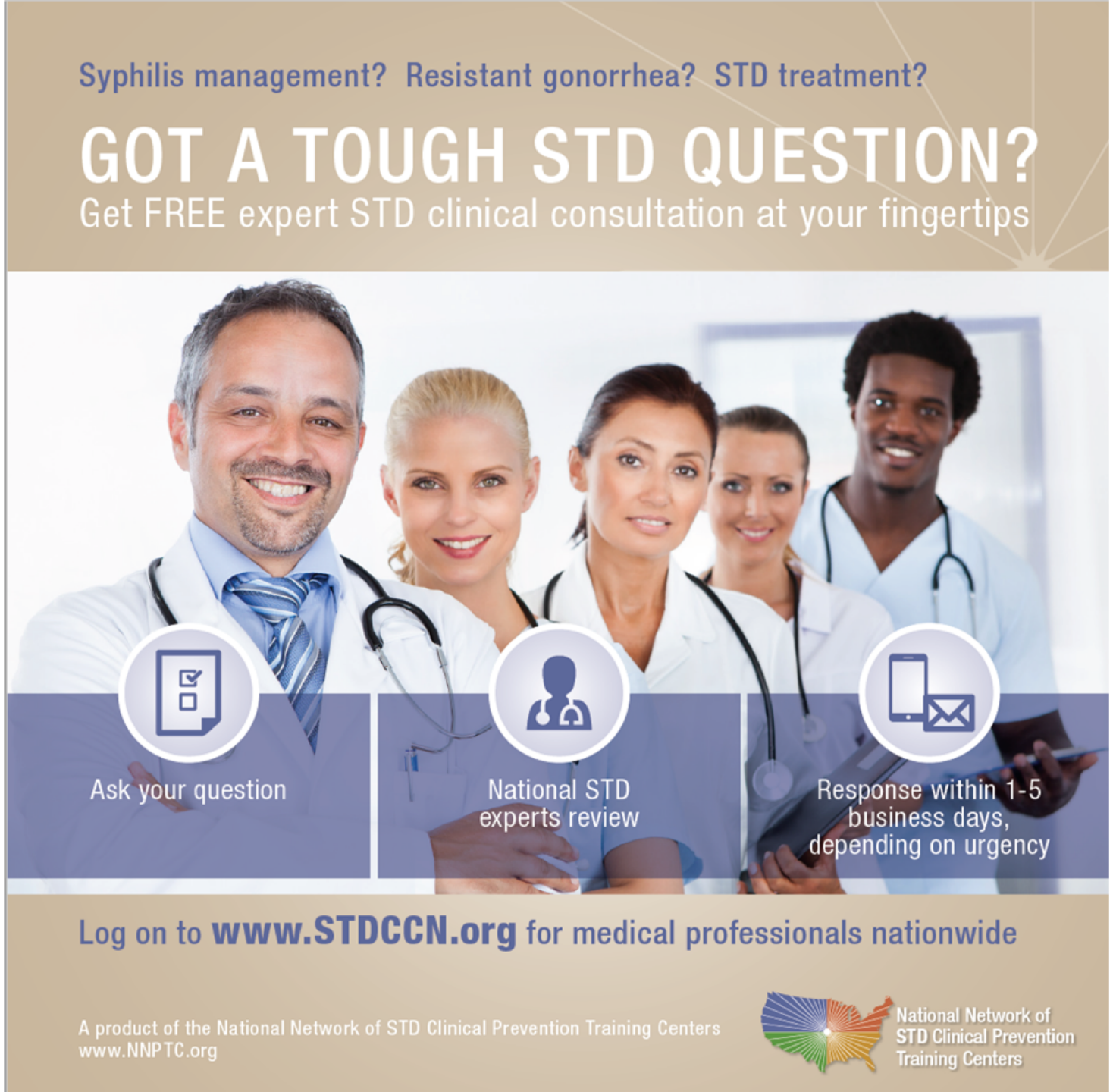
Disclosure

- Hillary Liss has no relevant financial relationships with an entity producing, marketing, re-selling, or distributing health care goods or services consumed by, or used on patients.



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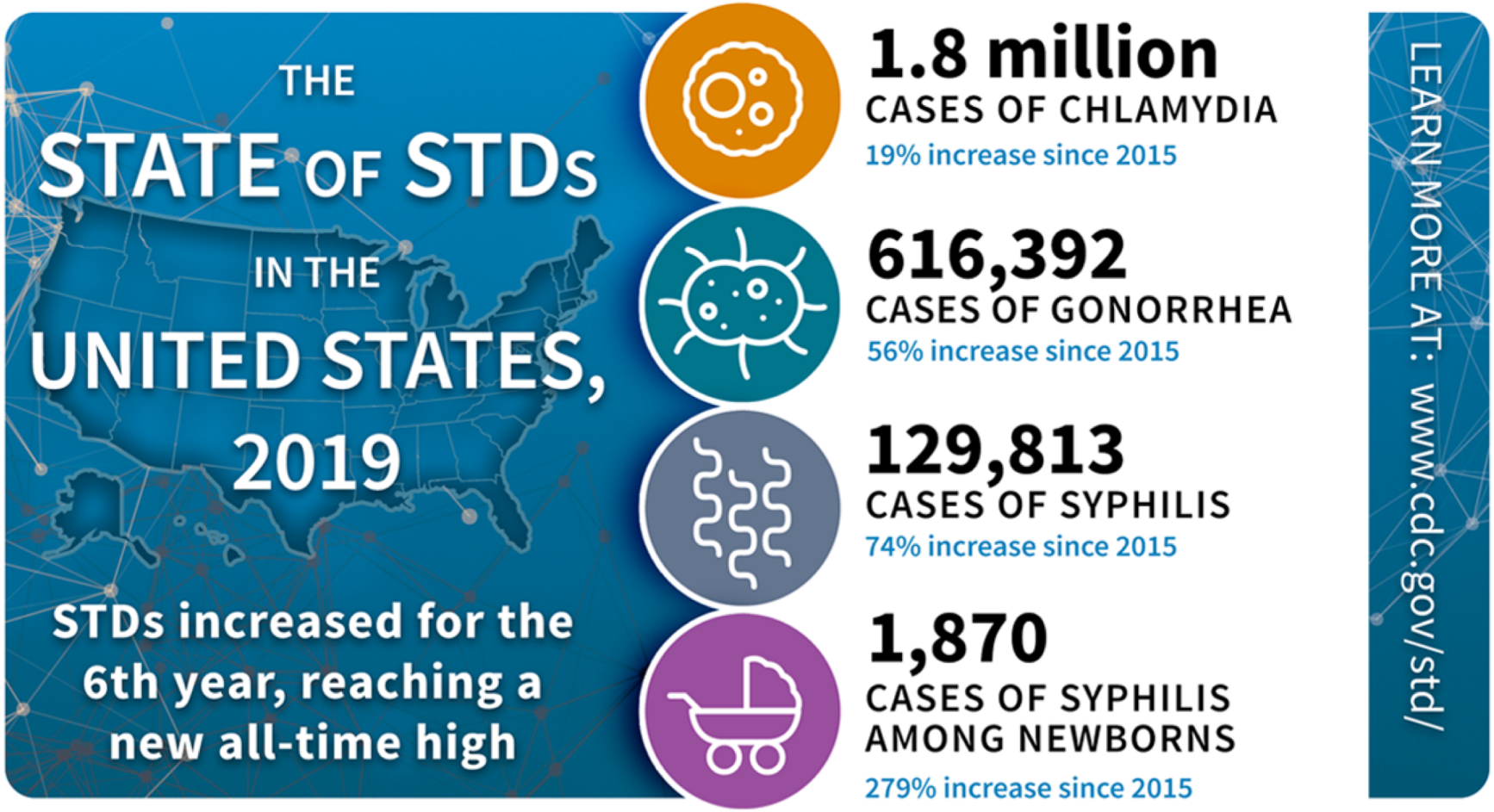
2019 was worst year on record for reported STIs



OVER HALF OCCURRED AMONG YOUNG PEOPLE 15-24 years of age

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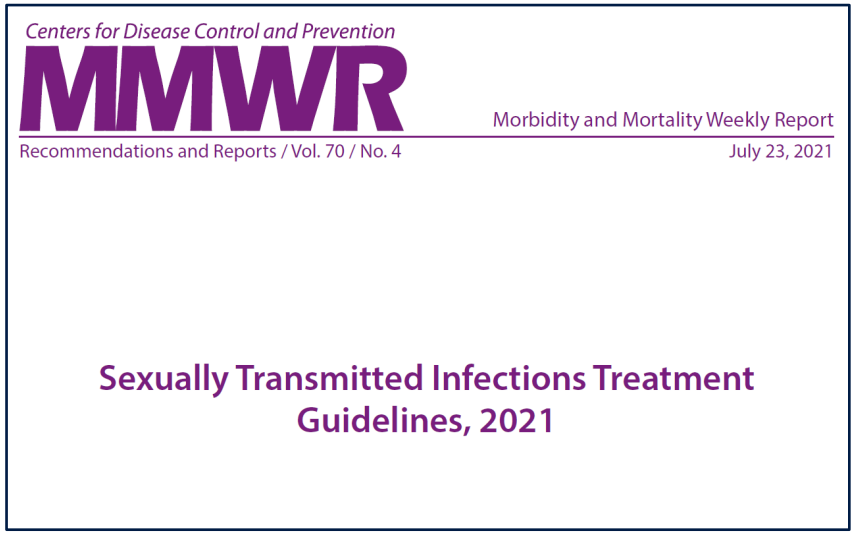
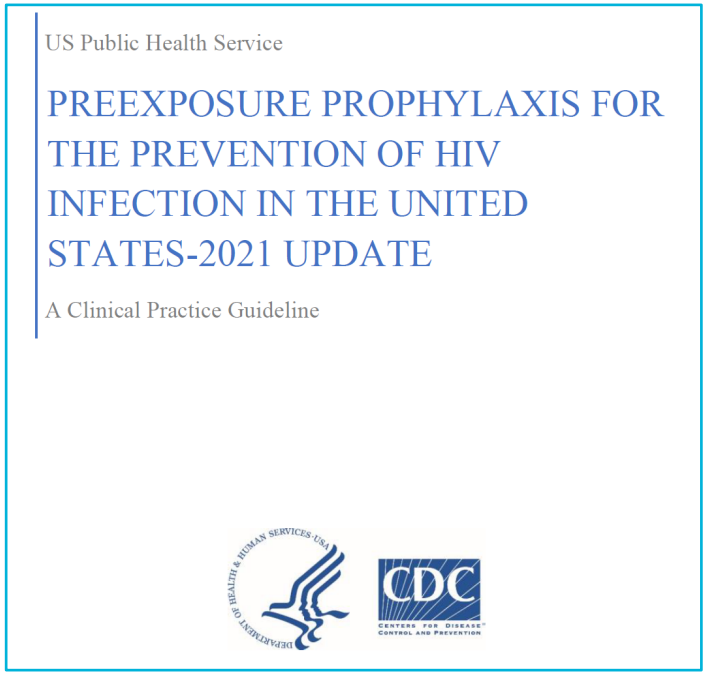
https://www.cdc.gov/std/statistics/2019/images/stateofSTDs-sm-1200x659-1.png

New guidelines



- Hot off the presses!
- July 23, 2021

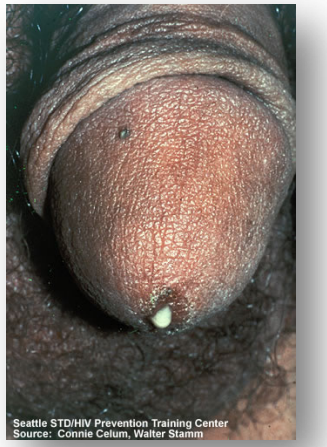


- Expected later in 2021

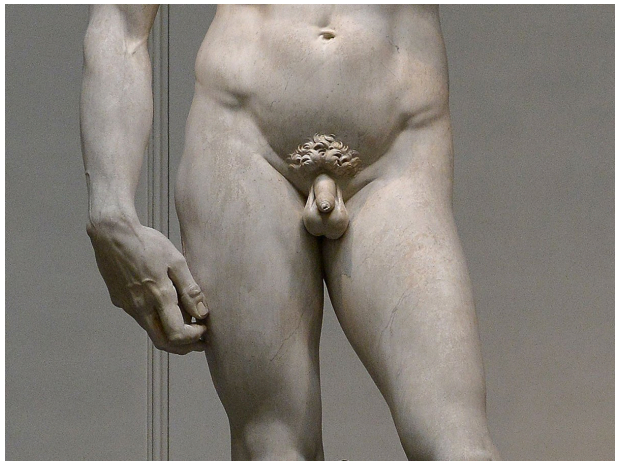
What's in a name?

STD vs STI

- Sexually transmitted disease
- Refers to disease state



- Sexually transmitted infection
- Refers to pathogen
- Often asymptomatic



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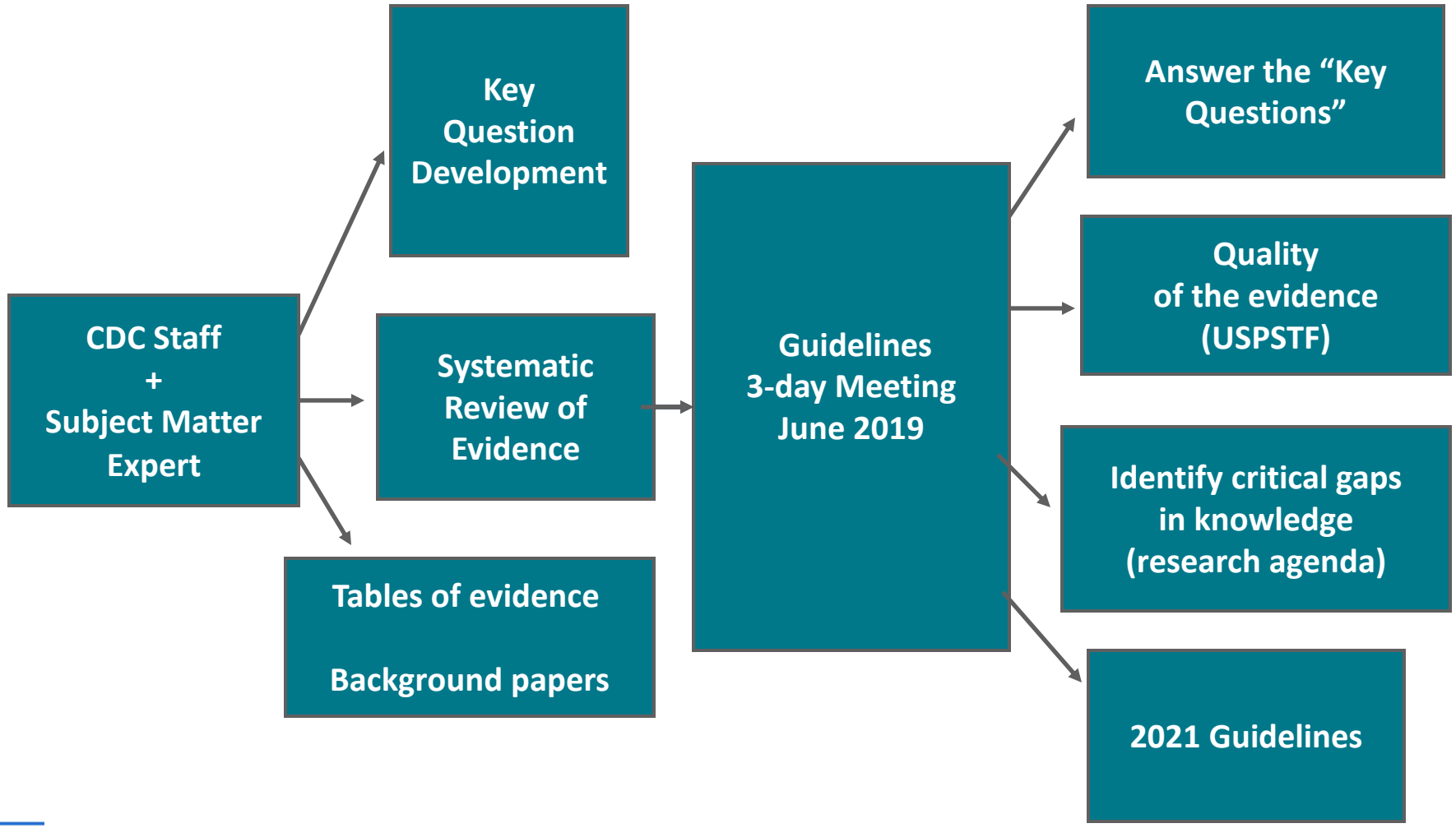
Evidence-based Approach to Guideline Development



CDC STI Treatment Guideline Development

- Evidence-based on principal outcomes of STI therapy
- “Recommended” regimens preferred over “alternative” regimens
- Treatments alphabetized unless there is a priority of choice
- Released July 2021
  - Available at: https://www.cdc.gov/std/treatment-guidelines/toc.htm
  - Interim app download: https://www.cdc.gov/STIapp/

Screening

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STI Screening for Cis-Women (WSM and WSW)

Women under 25 years of age

- Chlamydia/gonorrhea
- HIV at least once
- Hep C at least once if ≥ 18 yo (unless prevalence of Hep C < 0.1%)

Women 25 years of age and older

- Chlamydia/gonorrhea if at risk
- HIV at least once
- Hep C at least once (unless prevalence of Hep C < 0.1%)

Pregnant women

- Chlamydia (<25 years of age or risk and retest during 3rd trimester)
- Gonorrhea (<25 years of age or risk and retest during 3rd trimester)
- HIV
- Syphilis serology
- HepB sAg
- Hep C (unless prevalence of Hep C < 0.1%) WITH EVERY PREGNANCY

Screening not recommended for M. genitalium or trichomonas

STI Screening for Transgender Persons

Based on current anatomy and gender of sex partners

- Offer HIV screening to all transgender persons
- TG persons who have sex with cisgender men, at similar risk for STIs as cis-MSM

Transgender women post vaginoplasty

- GC/CT (all sites of exposure: oral, anal, genital)

(Urine vs neovaginal swab not specified, best specimen type based on tissue type used to construct neovagina)

Transgender Men post metoidioplasty

- If vagina still present and need to screen for STIs, cervical (or vaginal) swab should be used

STI Screening for cis-MSM

- HIV*
- Syphilis*
- Urethral GC and CT*
- Rectal GC and CT (if receptive anal sex)*
- Pharyngeal GC (if oral sex)*
- Hepatitis B (HBsAg, HBV core ab, HBV surface ab)
- Hepatitis C: (At least once if ≥ 18 yo, unless prevalence of infection < 0.1%)
- Anal cancer: annual digital anorectal exam may be useful (no anal Pap rec yet)
- HSV-2 serology (consider)

- At least annually, more frequent (3-6 months) if multiple/anonymous partners, drug use, or partners w/ risk
- Routine screening not recommended for M. genitalium

What about “Extragenital” Screening?

- Extragenital screening = testing for STIs at any body site other than genitourinary (urethral/urine/vaginal/cervix)
- Usually refers to rectal and oropharynx
- Typically for gonorrhea and/or chlamydia only
- Recommended routinely only for men who have sex with men (MSM), but now permissive for other individuals

Importance of Extragenital GC/CT Infections

- Transmission
  - 30% of symptomatic gonococcal urethritis is attributable to oro-pharyngeal exposure[1]
- HIV Transmission
  - Can potentiate acquisition, even after controlling for sexual behaviors[2-4]
- Treatment can differ
  - Pharyngeal GC[5]
    - Ceftriaxone > Cefixime
  - Rectal CT[6]
    - Doxy >>> Azithromycin

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1. Barbee et al, STI, 2015; 2. Vaughan, BMC Med Res Methodol, 2015; 3. Kelly, AIDS Res Hum Retroviruses, 2015; 4. Jin, JAIDS, 1999; 5. Moran, STD 1995; 6. Kong, JAC, 2015

Extragenital Gonorrhea & Chlamydia is Common

- Among MSM, high rates of extra-genital GC & CT
  - Pharyngeal GC: 9.2%[1]
  - Rectal GC: 9.7%[3]
  - Rectal CT: 12%[3]

- The majority of infections are asymptomatic
  - 92% of pharyngeal GC[2]
  - 84 - 86% of rectal GC[2]

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1. Kent CK. CID 2005
2. Morris, CID 2006
3. Barbee, STD 2014

Don’t forget the triple dip: STD Screening for MSM

Syphilis & HIV serology

Pharyngeal GC

Urine GC/CT

Rectal GC/CT

Annually for all sexually active MSM

Every 3-6 months for high-risk MSM

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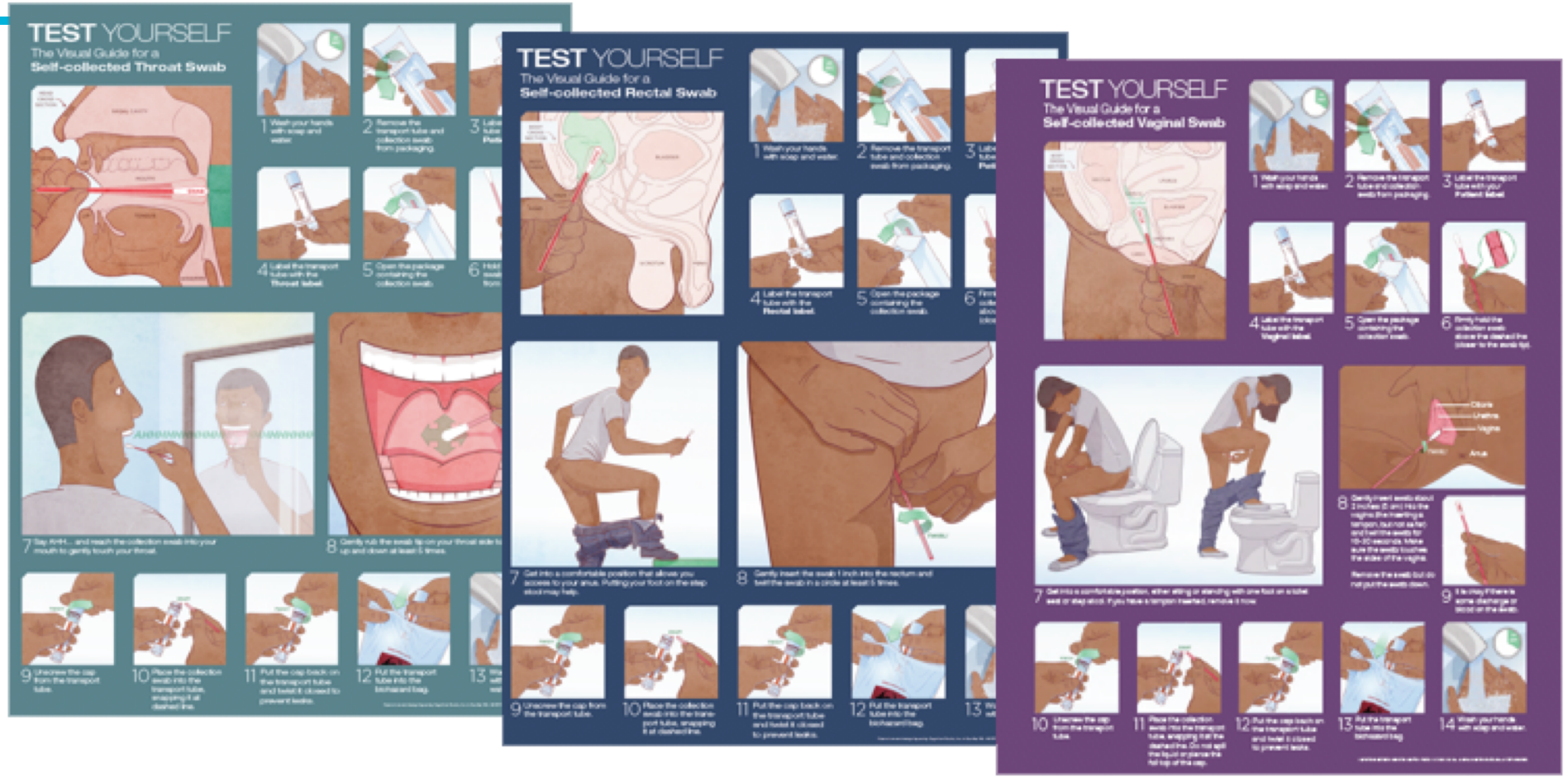
STI Self-Testing Program



Available in English and Spanish

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Email aradford@uw.edu or go to https://www.uwptc.org/visual-guides for free posters for your clinic

STI Screening for cis-MSW

- Routine STI screening not recommended
  - GC/CT recommended in high prevalence settings (e.g. adolescent clinics, correctional facilities, and STI clinics)
- HIV at least once (between 13-64 years of age)
- Hep C at least once if ≥ 18 yo (unless prevalence of Hep C < 0.1%)

Who should be Screened for CT/GC?

Females	• < 25 annually, 25+ if at risk • Pregnant <25 or risk
MSM	• 3-6 month intervals at all exposed sites: genital, rectal, pharyngeal
MSW	• High prevalence settings (e.g., Corrections, STI Clinics, adolescents)
Persons living with HIV	• At least annually • All exposed sites: genital, rectal, pharyngeal
Patients on PrEP	• Every 3-6 months • All exposed sites
Adolescents	• Consider rectal/pharyngeal screen based on reported behavior/ exposure

Who should be screened for Syphilis

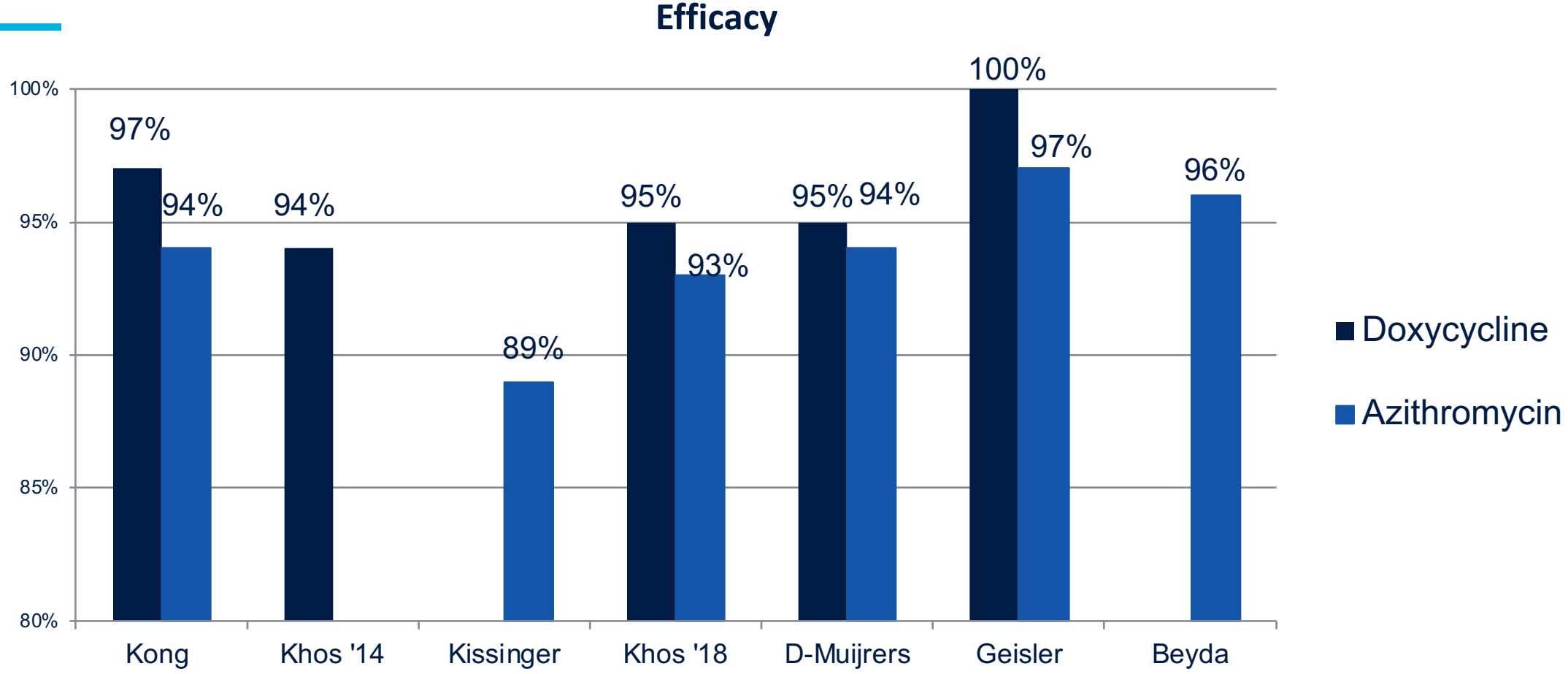
Pregnancy	• At first prenatal visit • Again at 28 weeks and at delivery (if at high risk, or residing in area with high syphilis morbidity)
MSM	• Including those on PrEP, 3-6 month intervals
Corrections	• Universal opt out screening on intake based on local area or institutional incidence
Persons living with HIV	• At least annually
STI Clinic patients	• Regardless of symptoms • If other STI diagnosed

Who should be screened for HIV?

- CDC recommends: At least one time screening for all patients aged 13-64 years
  - All persons who seek STI screening
- USPSTF recommends:
  - Screen people aged 15 to 65 years
  - Risk-based screening for younger adolescents & older adults
  - Pregnant women regardless of age

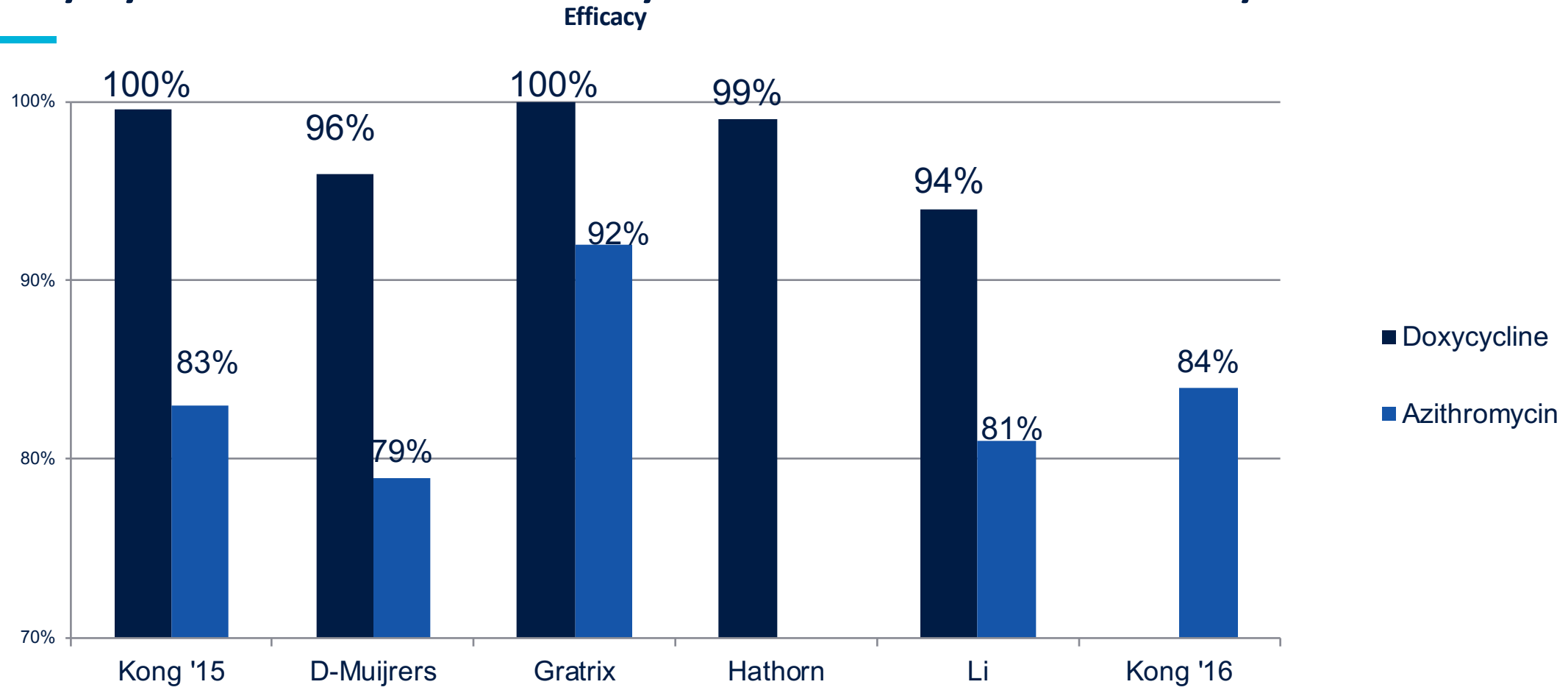
Chlamydia

Doxycycline vs Azithromycin for Urogenital Chlamydia



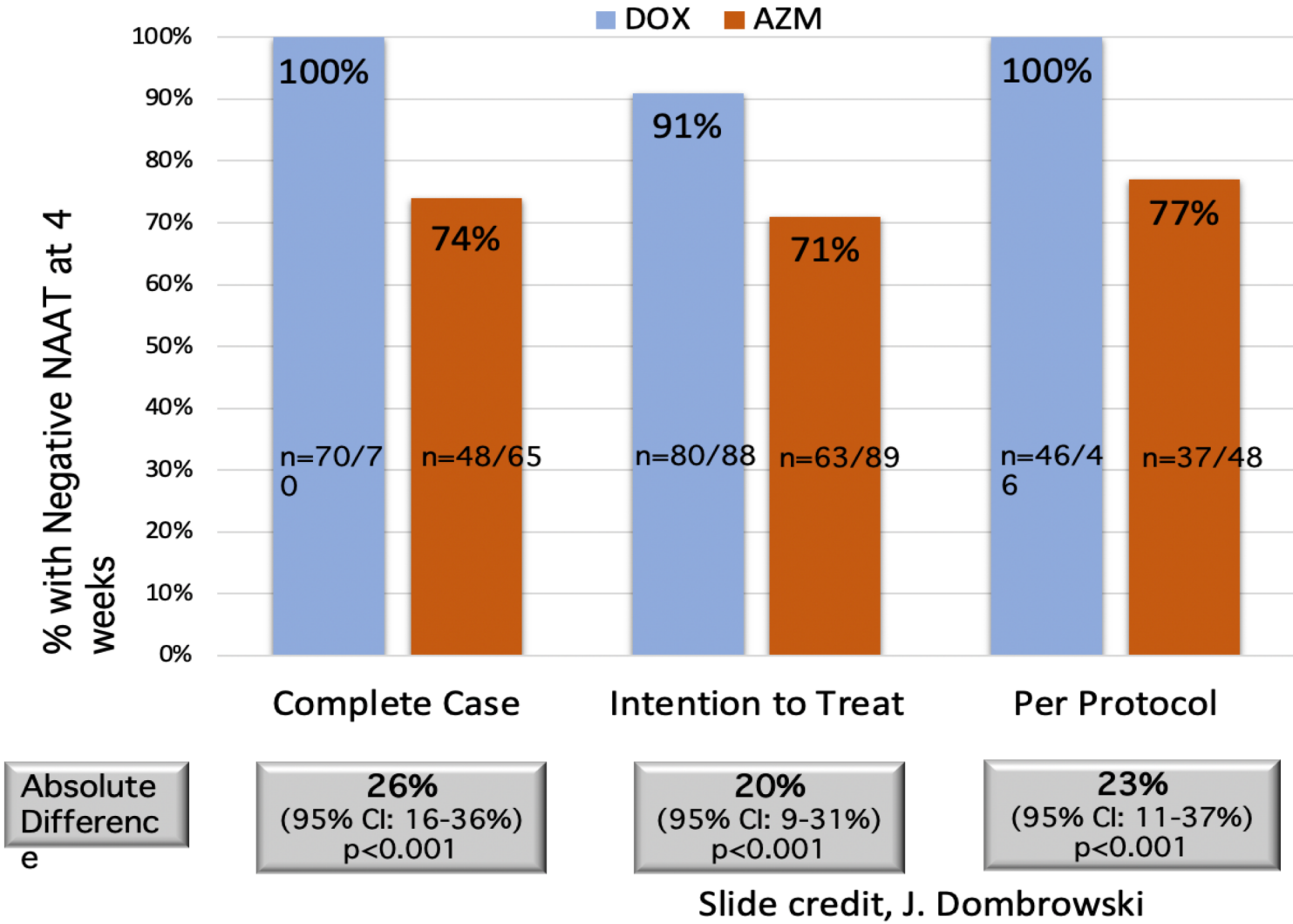
Slide credit: Dr. Will Geisler

Doxycycline vs Azithromycin for Rectal Chlamydia



Slide credit: Dr. Will Geisler

Randomized Controlled Trial DOX vs AZM for Rectal CT: Microbiologic Cure at 4 Weeks



Slide credit, J. Dombrowski

Dombrowski J, *2021, CID* https://doi.org/10.1093/cid/ciab153

Chlamydia Treatment:

Urogenital/ Rectal/ Pharyngeal

Change in 2021 STI Treatment Guidelines

Recommended regimens (non-pregnant):

- Doxycycline 100 mg orally twice daily for 7 days*

Alternative regimens (non-pregnant):

- Azithromycin 1 g orally in a single dose **OR**
- Levofloxacin 500 mg orally once daily for 7 days

*Doxycycline delayed-release 200 mg, once-daily dosing for 7 days effective for urogenital CT.
More costly but lower frequency GI side effects than standard doxycycline.

Chlamydia Treatment: Pregnancy

Recommended regimen (pregnant*):

- Azithromycin 1 g orally in a single dose

Alternative regimens (pregnant*):

- Amoxicillin 500 mg orally three times a day for 7 days

*** Test of cure at 3-4 weeks only in pregnancy**

Expedited Partner Therapy for GC/CT

- No states in US prohibit EPT (either allowable or potentially allowable by law/statute in all 50 states)
- Previously only recommended for hetero men/women, now "shared decision making" for EPT for MSM
- Providing patients with packaged oral medications is preferred approach
  - Partners (especially adolescents) may not fill prescriptions

Sure feels like there are a lot of changes for me in the 2021 CDC STI Guidelines!

Chlamydia

Hold my beer…

Gonorrhea

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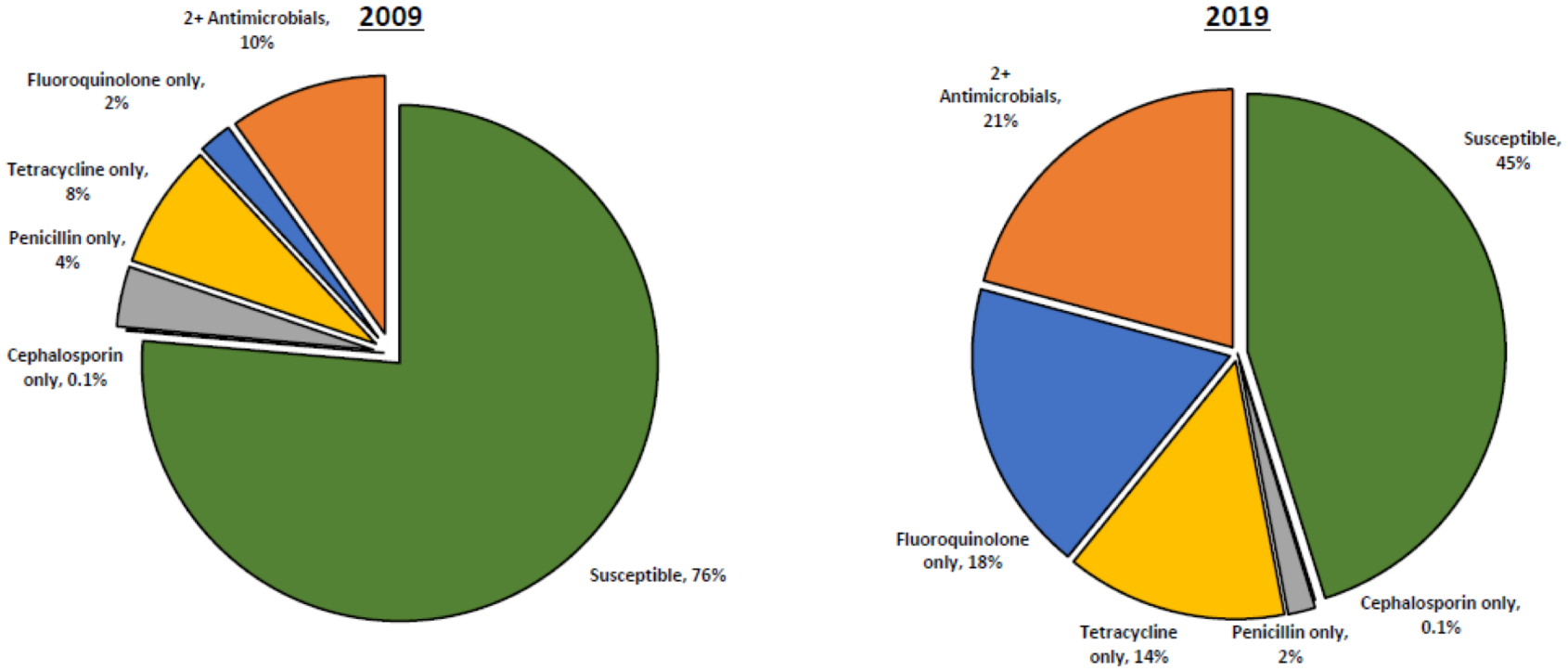
Gonorrhea

More than half of GC isolates are resistant to at least one antibiotic

Prevalence of Resistant or Decreased Susceptibility of *N. gonorrhoeae* Isolates to Antimicrobials, GISP, 2009 and 2019*



** 2019 data are preliminary*

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Slide courtesy Sancta St. Cyr
National STD Prevention Conference 2020

New Gonorrhea Treatment Guidelines

for uncomplicated infections

Ceftriaxone 500 mg IM x 1
for persons weighing <150kg*

*For persons weighing ≥ 150 kg, 1 g of IM ceftriaxone should be administered

However, if chlamydia has not been excluded, treat for chlamydia with:

Doxycycline 100 mg PO BID x 7 days

For pregnancy, allergy, or concern for non-adherence, 1 g PO azithromycin x 1 can be used

- No longer recommending dual therapy with azithromycin
- Test-of-Cure at 7-14 days post treatment for **pharyngeal** gonorrhea

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Update to CDC's Treatment Guidelines for Gonococcal infection, 2020; MMWR

New Alternative Gonorrhea Treatment

for uncomplicated infections of the cervix, urethra, and rectum **if ceftriaxone is not available**:

Cefixime **800** mg PO x 1

However, if chlamydia has not been excluded, treat for chlamydia with:

Doxycycline 100 mg PO BID x 7 days

For pregnancy, allergy, or concern for non-adherence, 1 g PO azithromycin x 1 can be used

Cephalosporin allergy: Gentamicin 240 mg IM + azithromycin 2 g PO

No reliable alternative treatments are available for **pharyngeal** gonorrhea

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Update to CDC's Treatment Guidelines for Gonococcal infection, 2020; MMWR

Rationale for GC Treatment Changes

- Improved antimicrobial stewardship
- Pharmacokinetic and pharmacodynamic considerations
- Changes in azithromycin susceptibility in GC

Antimicrobial Stewardship

Need to minimize antibiotic exposure unless benefit outweighs risk

Risk benefit of dual vs monotherapy for GC

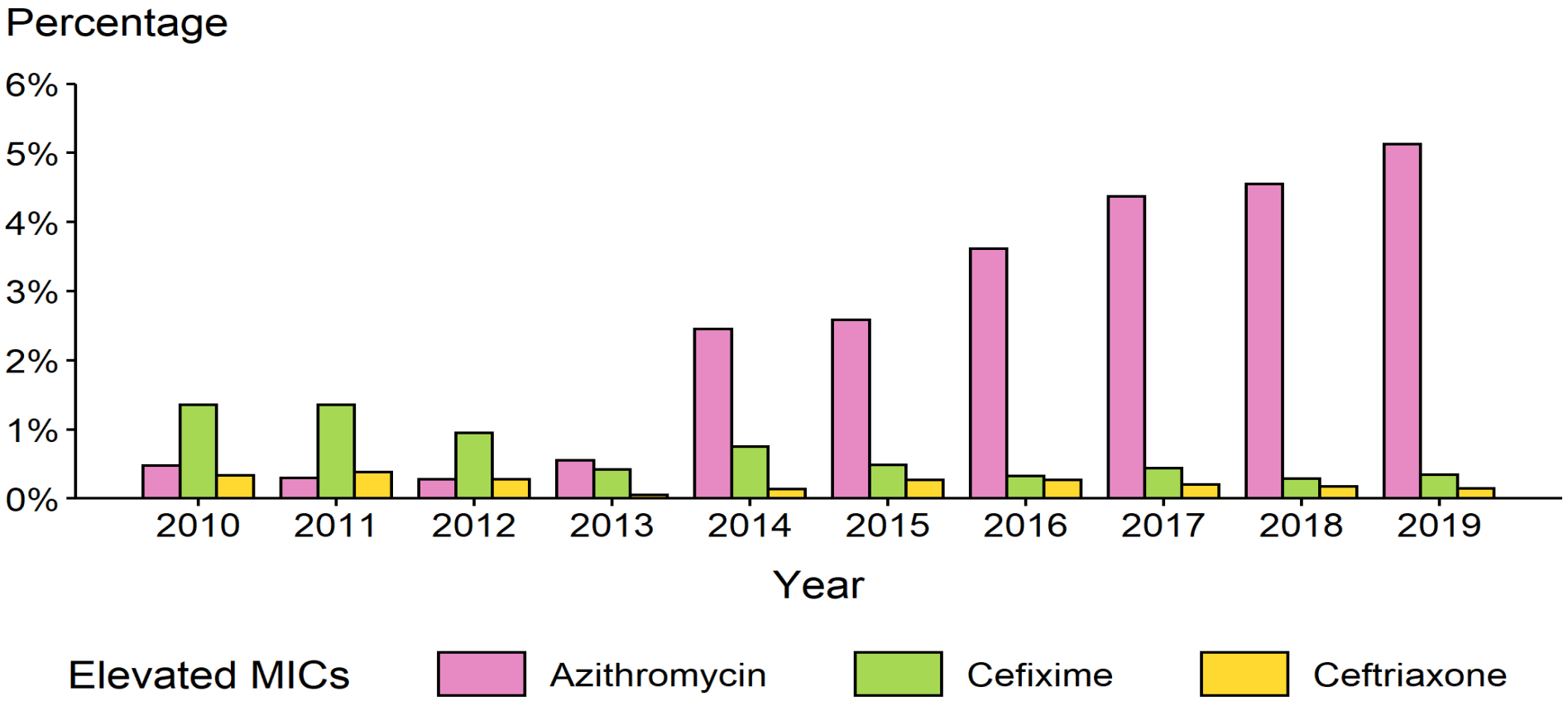
Drug-Resistant GC Urgent Threat

- Azithromycin resistance is a concern for other bacteria, so want to reduce overall use of azithromycin

Pharmacodynamics/ Pharmacokinetics

- Antibiotic most effective when drug levels are above MIC (minimum inhibitory concentration): lowest concentration of antibiotic needed to kill the bacteria
- Ceftriaxone kills GC when levels are high enough for long enough
  - 20-24 hours for Ceftriaxone
  - 500 mg dose most effective
  - Via modeling/mouse model
- Higher dose also more likely to kill gonorrhea in the pharynx

Rise in GC Isolates with Decreased Susceptibility to Azithromycin (~5%) Gonococcal Isolate Surveillance Project (GISP), 2010–2019



NOTE: Elevated MIC = Azithromycin: ≥ 2.0 µg/mL; Cefixime: ≥ 0.25 µg/mL; Ceftriaxone: ≥ 0.125 µg/mL

Mycoplasma genitalium

More than 1 in 4 men with urethritis have *Mycoplasma genitalium*

MAGNUM STUDY

Men with urethritis symptoms were enrolled from 6 U.S. STD clinics during 6/2017–8/2018

Study Site (n)	Prevalence of MG (95% CI)
Durham, NC (n=93)	24.7 (16.0–33.5)
Greensboro, NC (n=152)	38.8 (31.1–46.6)
Pittsburgh, PA (n=174)	27.6 (20.9–34.2)
Birmingham, AL (n=235)	29.8 (23.9–35.6)
New Orleans, LA (n=103)	29.1 (20.4–37.9)
Seattle, WA (n=157)	20.4 (14.1–26.7)
TOTAL (n=914)	**28.7 (23.8–33.6)**

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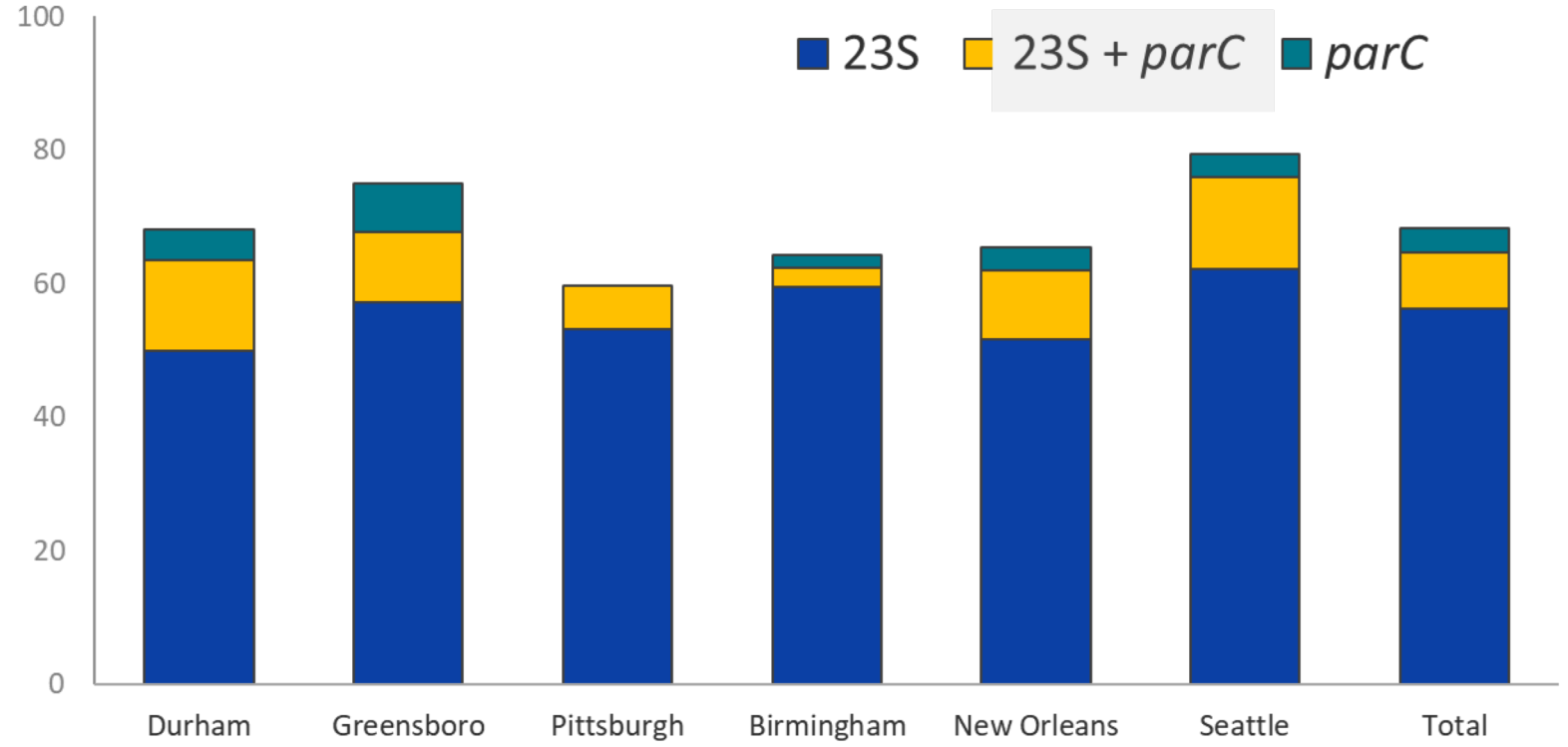
National Institutes of Health [HHSN2722013000121, HHSN272000010, DIMD16-0039]

Bachmann LH, Kirkcaldy RD, et al. CID 2020

M. genitalium screening and diagnostic testing

- Population based screening for M. genitalium is not recommended
- Diagnostic testing: NAAT (FDA approved in 2019) for urine, urethral, penile meatal, endocervical, vaginal specimens
- When to test: persistent urethritis that fails initial treatment, also consider for persistent PID or cervicitis

Over 50-60% of M. genitalium infections have reisistance mutations to macrolides (azithro)



National Institutes of Health [HHSN2722013000121, HHSN272000010, DIMD16-0039]

Bachmann LH, Kirkcaldy RD, et al. CID 2020

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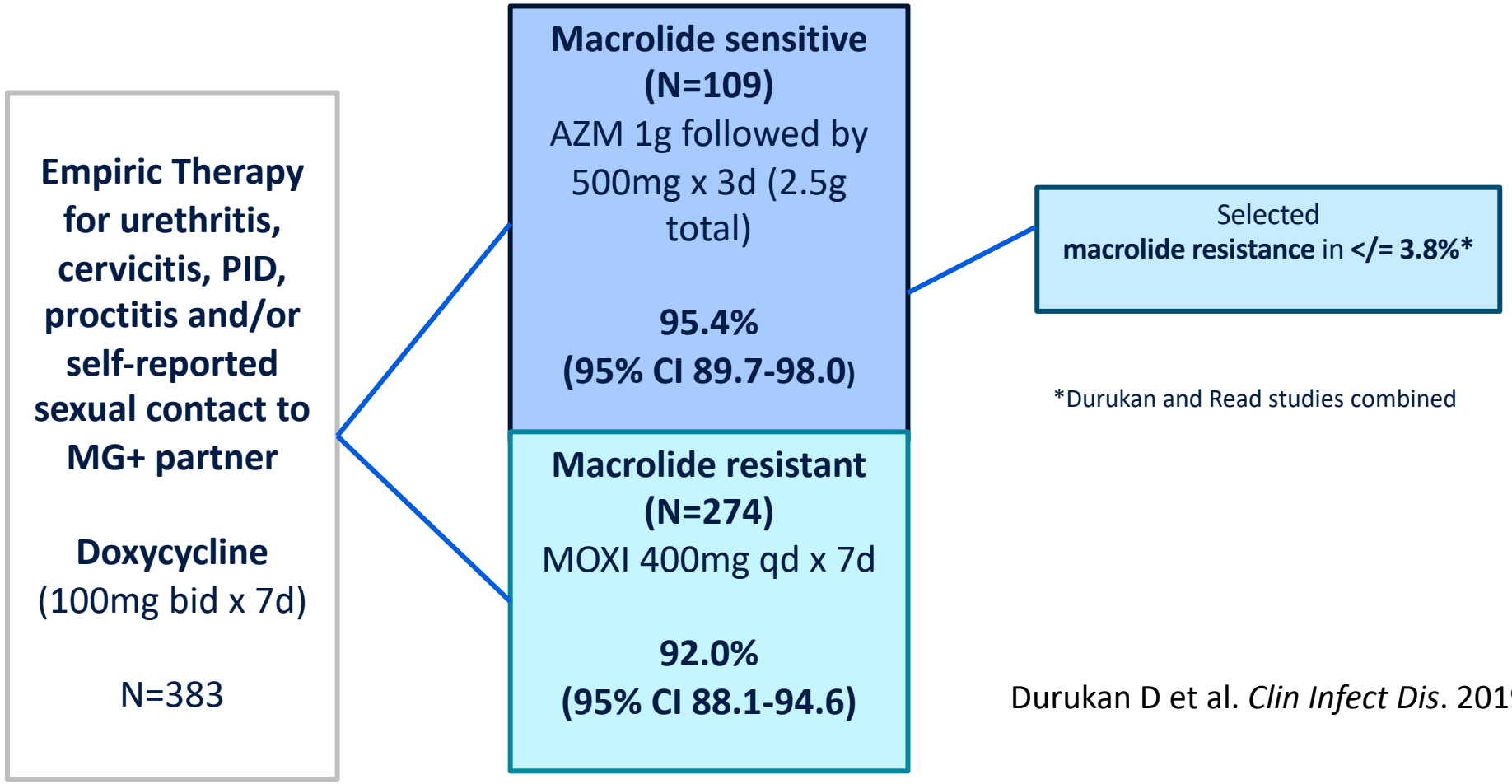
Slide credit: L Bachmann

Resistance guided therapy: *M. genitalium*



*Durukan and Read studies combined

Durukan D et al. *Clin Infect Dis*. 2019

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Slide credit: L Bachmann

M. genitalium Treatment

Change in 2021 STI Treatment Guidelines

- **Sequential treatment for suspected/documented M. genitalium**

Start with Doxycycline to reduce bacterial load

Doxycycline 100 mg BID x 7days → THEN → Moxifloxacin 400 mg BID x 7days

If local macrolide resistance is low or known macrolide sensitive

Doxycycline 100 mg BID x 7days → THEN → Azithromycin 2.5 gm over 4 days

(Azithromycin- 1 gm x 1day then 500 mg x 3day)

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Laura Bachmann. National STD Prevention Conference 2020, September 14-24,2020.

Trichomonas

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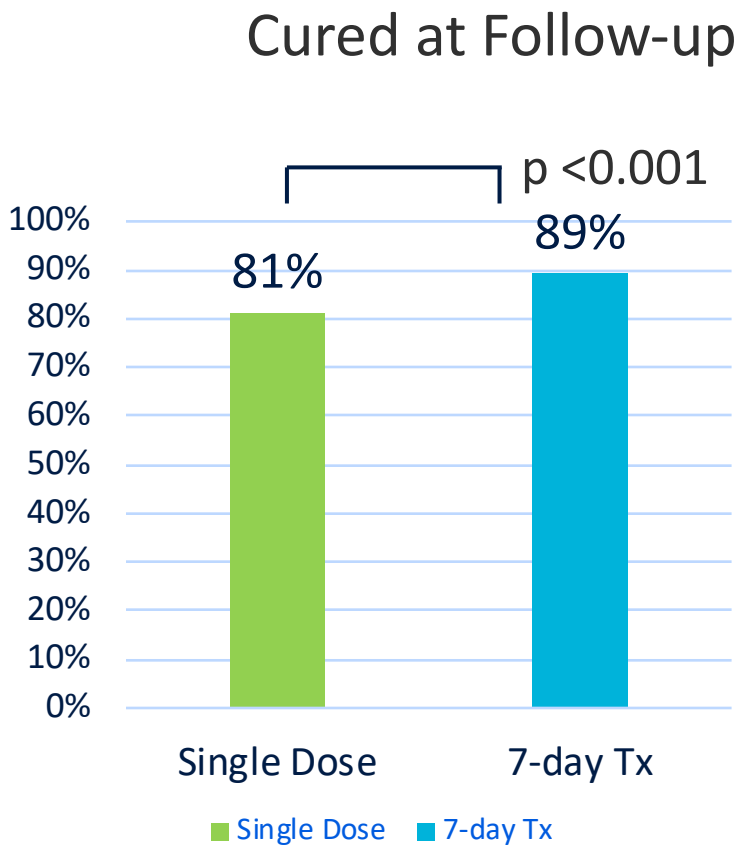
T. Vaginalis screening and diagnostic testing

- Screening for T. vaginalis is recommended for
  - Cis-women with HIV
  - Cis-women in correctional settings
  - Consider for other high prevalence settings
- Diagnostic testing: NAAT for urine, urethral, endocervical (including liquid cytology), vaginal
  - When to test: symptomatic patients

Treatment Consideration: Single dose metronidazole is not as effective as 7 days

- Single dose previously recommended for trich in HIV-negative women, 7-day therapy (500 mg BID) recommended for patients with HIV (CDC TX GL 2015)
- N=623 women randomized 1:1 to single dose MTZ vs 7 day
- Culture TOC, 6-12 days post treatment



Kissinger, 2018 Lancet Infect Dis

Trichomoniasis Treatment

Change in 2021 STI Treatment Guidelines

Recommended regimen: **Vaginal trichomonas (HIV+/HIV-)**

Metronidazole 500 mg PO BID x 7d

Metronidazole 2 g PO single dose for men w/ trichomonas or male partners)

ACOG 2020 Treatment Guidelines

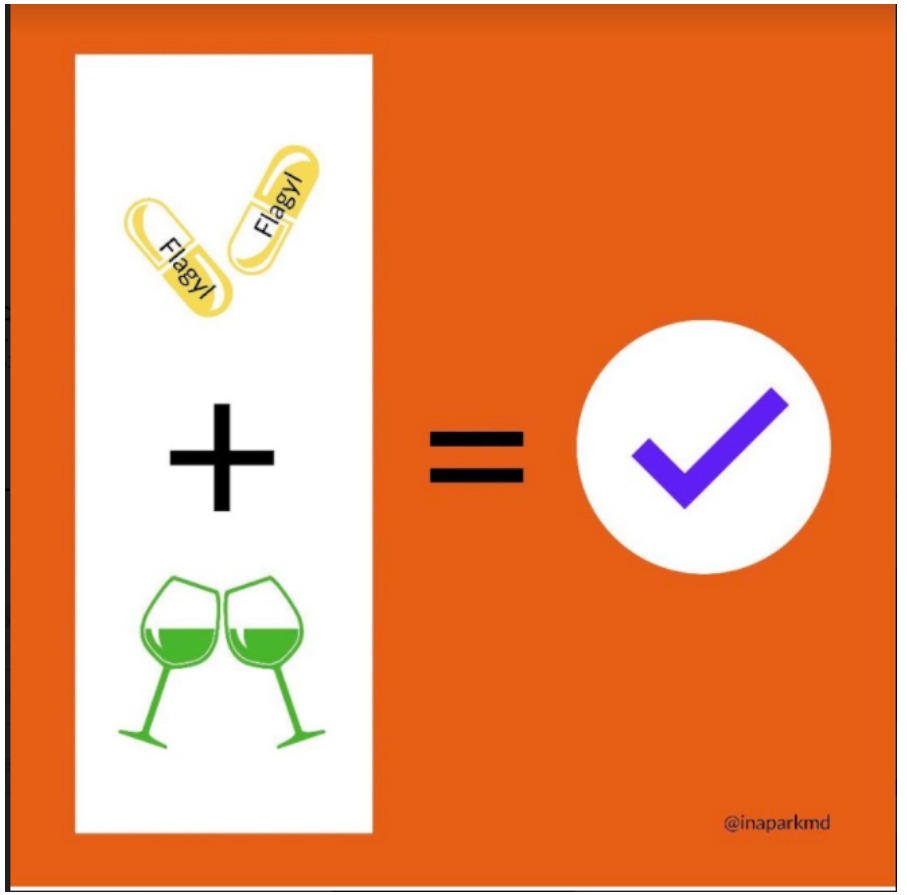
Metronidazole 500 mg PO BID x 7 d

CDC 2015 STD Treatment Guidelines,
ACOG Practice Bulletin 215. OB/GYN Vol 135. Jan 2020

Metronidazole and Alcohol

Change in 2021 STI Treatment Guidelines

- Metronidazole does not actually inhibit acetaldehyde dehydrogenase (as occurs with disulfiram)
- Evidence review: no in vitro or clinical studies, no animal models, and no adverse event reporting
- Refraining from ETOH is unnecessary during treatment



2021 CDC STI Treatment Guidelines

Fjeld H, Raknes G. Tidsskr Nor Laegeforen. 2014;134(17):1661–3

Test of Cure vs Retesting

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Test of Cure vs Retesting

TEST OF CURE	Time period	Who
GC (pharynx)	2 weeks	All patients
CT (cervix)	4 weeks	Pregnant patients only
LGV (all sites)	4 weeks	If AZM used instead of DOX (consider)
M. genitalium	3 weeks	If DOX + AZM used instead of MOXI

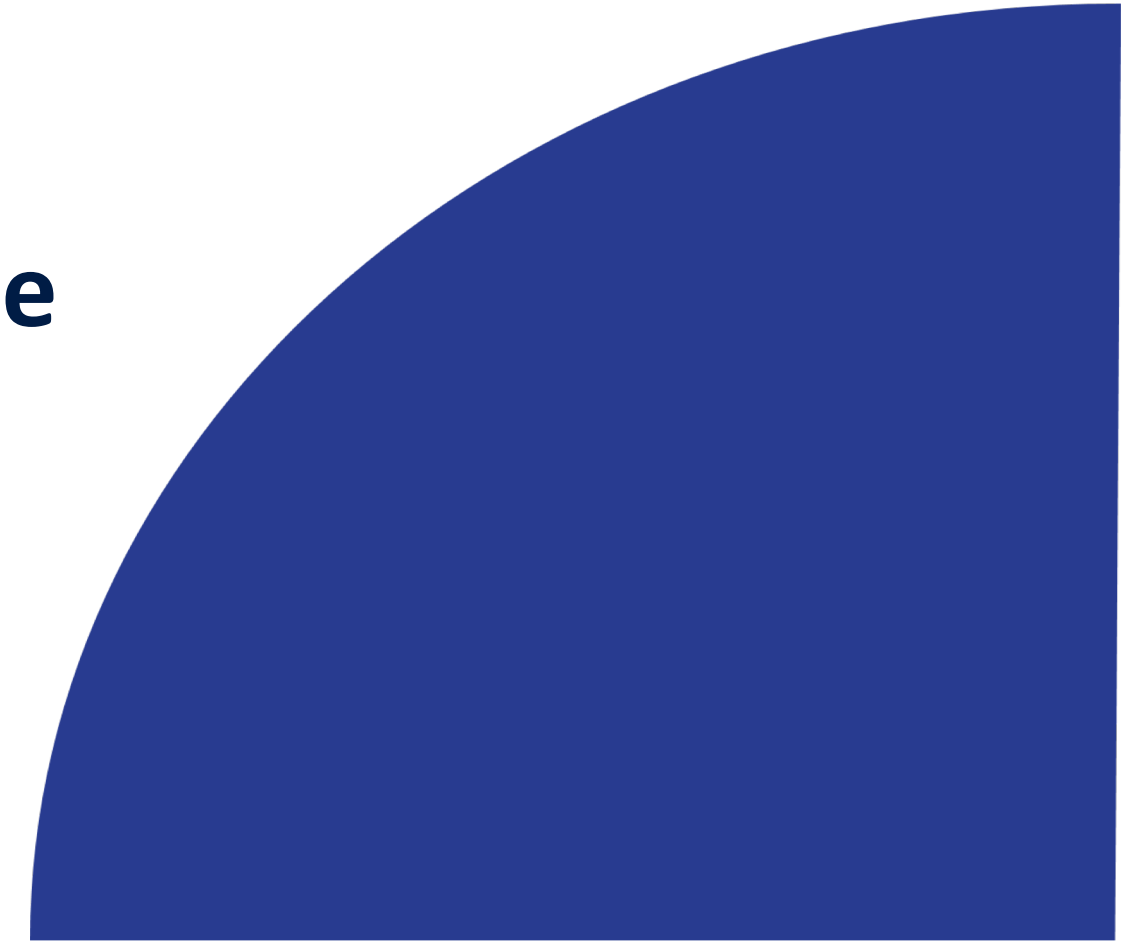
RETEST FOR REINFECTION	Time period	Who
GC/CT/LGV (all sites)	3 m (anytime from 1-12 m ok)	All patients
Trichomonas	3 m (anytime from 1-12 m ok)	Patients w/vaginal infection

Syphilis

Syphilis Diagnosis and Treatment

- Neurosyphilis Dx in pts with reactive serology and…
  - Ocular symptoms: if isolated ocular sx, no CN or other neuro involvement, **and** confirmed eye abnormalities on exam, no CSF exam needed before tx
  - Otosyphilis: if isolated auditory abnormalities, CSF likely to be normal, no CSF needed before tx
- Follow up: if RPR drops appropriately and patient improves clinically, no repeat CSF needed for pts without HIV or patients with HIV on ART
- Treatment: no changes for any stage of syphilis

Pelvic Inflammatory Disease



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PID Outpatient Treatment: Should Metronidazole be used routinely?

- Randomized Controlled Trial (N=233 cis women)
- Ceftriaxone 250 mg IM **plus** Doxcycline 100 mg PO BID x 14 days
  plus
  - Metronidazole 500 mg BID x 14 day **OR**
  - Placebo BID X 14 day
- Primary outcome: Clinical improvement 3 days
- Additional outcomes: Anerobic organisms in endometrium at 30 days, fever, CMT reduction

Wiesenfeld et al. CID 2021

Study Results

- Clinical improvement at 3 days similar between two arms
- Metronidazole
  - Reduced anaerobes in endometrium (8% vs 21%, $p<0.05$)
  - Reduced M. genitalium (cervical) (4% vs 14%, $p<0.05$)
  - Reduced CMT/pelvic tenderness (9% vs 20%, $p<0.05$)

- **Conclusion: Metronidazole should be routinely added for PID RX**

Wisenfeld et al. CID 2021

PID IM/Oral Treatment Regimens: Metronidazole for all

Change in 2021 STI Treatment Guidelines

Oral regimens:

- Ceftriaxone 500 mg IM (or other parenteral 3rd generation cephalosporin) x 1 ***or***
- Cefoxitin 2 g IM ***with*** probenecid 1 g orally once

  PLUS

- Doxycycline 100 mg orally twice daily for 14 days

  WITH ~~OR WITHOUT~~

- Metronidazole 500 mg orally twice daily for 14 days

Acknowledgments

- Ina Park- UCSF, California Prevention Training Center
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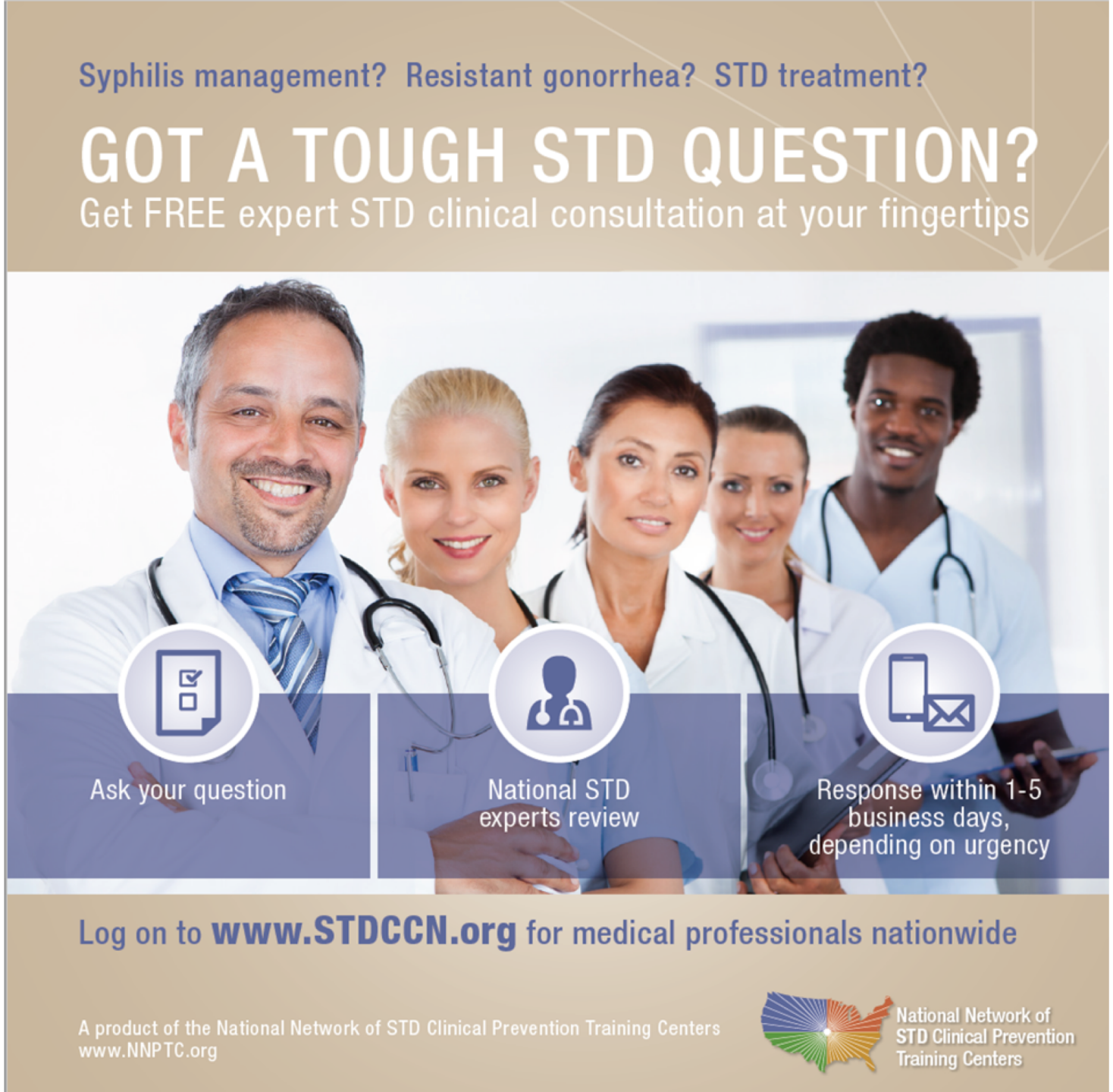
- Sancta St. Cyr- CDC
- Will Geisler- University of Alabama Birmingham
- Sharon Adler- UCSF, California Prevention Training Center
- Chris Fox- OHSU



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Thank you!!

Any Burning Questions?

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